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FEDESA
BRUSSELS

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Dear Colleagues

RE: VICH – WG Biologicals Quality Monitoring – Extraneous Virus Test

Please may I have your attention for the following:

1. The Guideline for Extraneous Agents Testing.

After the meeting in Brussels I made a new draft of the Guideline for the test on Extraneous Agents in which I incorporated the comments made during the meeting of the Working Group.

You will note that the text has changed considerably. This was mainly caused by the fact that all statements which can potentially be considered as regulatory requirements had to be removed, as was suggested by Dr. Peter Castle. There may be still a few statements left which on the one hand may be considered as regulatory statements, but on the other hand can be considered as information. I have put these statement between [...].

I hope that the text now makes it absolutely clear that the guideline is intended only to describe methods of testing.

This approach also solves the important problem expressed by the Japanese representatives in respect of the difference in emphasis on in-process testing and finished product testing between Japan and the other regions. The new draft text of the guideline now only describes the technical aspects of the testmethod. It does not state when and where the test has to be applied. This will be the responsibility of the regulatory authorities.

I would very much appreciate if you could give your opinion and comments on the document. The document can than be amended in respect of those points on which agreement exists. This will leave more time to discuss the remaining unresolved issues during the meeting in Ames.

2. The guideline for testing of avian vaccines.

During the first meeting of the Working Group in Tokyo it was decided, on the proposal of Dr. Itoh, to limit the discussion to the test on extraneous viruses for mammalian vaccines produced on established cell lines.

After consultation of Dr. Itoh I now also prepared a document to serve as a the basis for discussion of the harmonisation of the tests to determine the presence of extraneous viruses in avian vaccines.

These papers contain a comparison between the following test methods, presently being used in the different regions:

1. The test for extraneous viruses in avian vaccines using embryonated eggs
2. The test for extraneous viruses in avian vaccines using cell-cultures
3. The test for extraneous viruses in avian vaccines using chickens.

This information is presented in a tabular form.

It is important to note that these testmethods are not only relevant for avian vaccines but also for mammalian vaccines, e.g. when the vaccine virus used for production may be potentially contaminated with avian viruses, because they were passaged in avian cells.

I would also like to have your opinion on these papers, especially to check whether or not the analysis is correct and complete. If I receive the comments in time, it will be possible to amend these tables and to make a draft text for the guideline. The remaining controversial points can than be discussed in Ames.

3. The scope of the guideline.

After intensive consultation with Dr.Itoh it is proposed not to make one single all compassing guideline for the tests on extraneous agents but to make a number of separate documents, which can be dealt with separately.

The guideline could have as main title:

**GUIDELINE FOR THE TESTS TO DETERMINE THE PRESENCE OF
EXTRANEIOUS AGENTS IN VETERINARY VACCINES.**

This guideline would consist of three separate documents:

Document 1.

A. Mammalian viral vaccines produced in established cell-lines.

Part I. Tests to determine the presence of extraneous viruses.

Guideline for the tests to determine the presence of extraneous viruses in mammalian viral vaccines produced in established cell-lines.

Document 2.

A. Mammalian viral vaccines produced in established cell-lines.

Part II. Tests to determine the presence of extraneous agents other than viruses.

Guideline for the tests to determine the presence of extraneous agents other than viruses in mammalian viral vaccines produced in established cell-lines.

Document 3.

B. Avian vaccines.

Guideline for the tests to determine the presence of extraneous agents in avian viral vaccines.

The following arguments are put forward to support this proposal:

- The reason why the guideline shall be limited to **mammalian** and **avian** viral vaccines is that these vaccines form the most important category of veterinary vaccines.
- The reason why the guideline shall be limited to **viral** vaccines only is that the tests used are very similar and are all based on the use of live cells e.g. cell cultures, embryonated eggs.
- The reason that the guideline shall be limited to extraneous **viruses** is that this category of agents is the most important.
- The reason that **bacterial** vaccines shall be excluded from the present guideline is that the purity of bacterial seeds can be determined without resorting to the use of cell cultures, except for organisms as Chlamydia which need living cells for reproduction.
- The test methods to detect the presence of for **non-viral** agents are very much dependent on the type of agent for which the test is intended and

very varied in nature and technique. In principle its scope can be limited to those agents which will not be detected with the normal sterility test method. This testmethod has already been agreed upon by the Japanese Pharmacopoeia, USP and Eur. Ph.

- The test for extraneous agents in **fish** vaccines are a very specific category which can be dealt with in a separate guideline.

These three separate, but related documents, can be dealt with separately in the VICH process. This approach will probably make it possible to have concrete results much earlier.

This proposed limited scope of the documents would have the important practical and political advantage that it will be possible to have it ready within a reasonable time. From the experience gained so far it is clear that the completion and agreement of a guideline which deals with all aspects of extraneous agents testing for all sort of vaccines will probably take years. That is an undesirable situation.

This proposal to split the document has still to be decided upon during the next meeting in Ames. However, to facilitate the discussion on the different subjects covered by each document I have already prepared separate documents. If necessary they can easily be put together again in one single document.

I am looking forward to your views on the matter.

With best wishes and kind regards,

Christiaan Folkers